REMARKS

Applicants thank Examiner Clow and Primary Examiner Moran for their time and courtesies extended to Applicants' representatives during the Interview of May 18, 2004. Applicants believe that the Interview has advanced prosecution of the present application. Generally, various ways of addressing the sole rejection were discussed during the interview.

It is respectfully requested that the present Amendment be entered into the Official File in view of the fact that the Amendment places the application into condition for allowance.

Claims 35, 44 and 48 as amended present no new issues requiring further search or consideration because claims of the same or similar scope have previously been presented and subsequently examined. In fact, the amendments to the claims are merely editorial in nature, and no new matter has been added. Thus, though the present reply is under 37 C.F.R. § 1.116, the present amendments to the claims raise no new issues.

In the alternative, if the Examiner continues with the rejections of the present application, it is respectfully requested that the present Amendment be entered for purposes of an Appeal since these claim amendments are merely editorial in nature and raise no new issues.

Claims 35-61 are pending in the present application, wherein claims 35, 44 and 48 have been amended (which are editorial in nature as mentioned above) and claims 46, 47, 58, 60 and 61 have been canceled without prejudice or disclaimer of the subject matter contained therein.

Claims 44-45 stand withdrawn from consideration, but rejoinder of these claims are respectfully requested. Claims 42, 43, 48-57 and 59 have been allowed.

Only a rejection of claims 35-41 is outstanding and addressed herein by Applicants. Applicants note that the present amendments to claims 35, 44 and 48 are clarifying in nature and not narrowing in scope. By clarifying the claimed invention, Applicants in no way are conceding any limitations with respect to the interpretation of the claims under the Doctrine of Equivalents. Applicants add that the amendment to claim 48 does not change the previously considered scope of this claim, wherein "containing" has the same meaning as "comprising".

Based upon the above considerations, entry of the present amendment is respectfully requested. Further, in view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Substance of the Interview

In accordance with M.P.E.P. § 713.04, Applicants provide the following remarks.

The May 18, 2004, Interview involved a discussion of withdrawing the finality of the Office Action as mentioned below, as the present rejection is based on new grounds not necessitated by Applicants' prior Amendment. Also, Applicants pointed to certain parts of the present

specification that together with the state of the art evidence sufficient enablement of the present invention. For instance, Applicants referred to working examples, pages 13-14 and Table 2 (at page 20) as evidence of how the present inventors have guided the skilled artisan in making and using the present invention. Table 2 shows, e.g., ELISA results illustrating a useful diagnostic peptide. The working examples describe how to make a peptide and test it for efficacy as a diagnostic reagent. Applicants also discussed the possibility of rejoining certain subject matter should the Examiner find allowable subject matter in the disputed claims (claims 35-41). Thus, Applicants herein request rejoinder of the withdrawn subject matter of claims 44-45.

Improper Finality

Applicants respectfully submit that the finality of the Office Action should be withdrawn since issues in the outstanding Office Action are newly cited and Applicants have not had a previous opportunity to address these issues. Further, these new issues are not a result of any amendments to the claims by Applicants.

Specifically, the Final Office Action of December 17, 2002 rejected some of the pending claims under 35 U.S.C. § 112, first paragraph, for asserted lack of enablement. The December 17th Office Action referred to the *Wands* factors and generally stated that one skilled in the art can diagnose aspergillosis only with undue experimentation. For example,

reference was made to how "no comparable methods for aspergillosis confirmation or diagnosis have been established" and "there is no way a priori of predicting actual diagnostic levels" (see Office Action at page 6, lines 2-4 and 10-11; see also page 5, lines 15-22 questioning diagnostic levels in Applicants' specification; see also page 6, lines 13-14 stating that "the values for diagnosis [in the specification] are not disclosed"). Thus, Applicants responded by filing a Rule 132 Declaration and appropriate arguments for patentability addressing these issues.

However, the present Office Action dated March 9, 2004, which is final, rejects claims 35-41 under 35 U.S.C. § 112, first paragraph, for asserted lack of enablement for different reasons. Specifically, the March 9th Office Action cites the *Wands* factors but questions how an amino acid sequence encompassing more than SEQ ID NOS: 1-6 can be used (see, e.g., page 4, lines 1-3 and 4-6).

Thus, the first Office Action of December 17 related to enablement from the standpoint of an ELISA value that is diagnostic, and the current Office Action relates to operability of peptides used for diagnosis. The current rejection was not necessitated by Applicants' amendment, and Applicants respectfully submit that the instant rejection in the current, outstanding Office Action is essentially a new rejection which Applicants address herein for the first time. Accordingly,

Applicants respectfully request withdrawal of the finality of the current Office Action.

Issues Under 35 U.S.C. § 112, First Paragraph

Claims 35-41 stand rejected under 35 U.S.C. § 112, first paragraph, for asserted lack of enablement. Applicants respectfully traverse, and reconsideration and withdrawal thereof are respectfully requested.

The Present Specification and the State of the Art Enable One Skilled in the Art to Make and Use the Presently Claimed Invention

The Office Action addresses the *Wands* factors, which are as follows:

1) the quantity of experimentation necessary;

2) the amount of direction or guidance presented;

3) the presence or absence of working examples;

4) the nature of the invention;

5) the state of the prior art;

6) the relative skill of those in the art;

7) the predictability or unpredictability of the art; and

8) the breadth of the claims.

See In re Wands, 858 F.2d 731; 8 USPQ2d 1400 (Fed. Cir. 1988); *see also* M.P.E.P. § 2164.01(a).

Applicants submit that all *Wands* factors and all evidence of patentability must be considered, wherein any conclusion of enablement or nonenablement must be based on the evidence as a whole. 8 USPQ2d at 1404, 1407; *see also* M.P.E.P. § 2164.01(a). Here, presently pending claim 35 in part defines that the peptide comprises the amino acid sequence of one of SEQ. ID. NOS.: 1-6. In consideration of the claimed invention with respect to the disclosure in the present specification and the state of the art, Applicants respectfully submit that a proper weighing of the *Wands* factors weighs in Applicants' favor. There is sufficient enablement of the claimed invention as follows.

The Nature of the Invention

The present invention involves quantitating the amount of peptide-IgG/IgE complexes and diagnosing aspergillosis based on the amount of peptide-IgG/IgE complexes. More specifically, the present invention is directed to a method for diagnosing aspergillosis in a patient, which comprises the steps of: incubating a body fluid sample from a patient with an ELISA plate having at least one peptide bound thereto; removing the body fluid sample from the ELISA plate; incubating the ELISA plate with anti-human IgG/IgE to form peptide-IgG/IgE complexes; removing IgG/IgE not bound in a complex; quantitating an amount of peptide-IgG/IgE complexes; and diagnosing aspergillosis based on the amount of peptide-IgG/IgE complexes. The at least one peptide is a peptide

comprising an amino acid sequence of one of SEQ ID NOS: 1, 2, 3, 4, 5 or 6.

The quantity of experimentation necessary

The Examiner has not pointedly discussed this factor in the Office Action. However, Applicants respectfully submit that this factor alone is not determinative of enablement for the present invention and that such experimentation as is required is not greater than typical in the art.

Relative level of skill in the art and breadth of the claims

Applicants and the Examiner seem to be in agreement that the level of skill in the art is high. Applicants also respectfully refer the Examiner to the previously filed Rule 132 Declaration as further evidence of this.

The claims seem somewhat broad with respect to the reagent used to determine the diagnosis of aspergillosis (*i.e.*, a peptide comprising an amino acid sequence of one of SEQ ID NOS:1-6).

The state of the art, the amount of direction or guidance presented, the presence or absence of working examples and predictability in the art

Applicants respectfully submit that the present specification gives ample guidance for making and using the presently claimed invention at pages 13-14. From this part of the present specification, one skilled in the art would recognize that various epitopic proteins have been screened, and are found to be operable as shown in Table 2 at page 20 of the present specification. Table 2 as mentioned displays the relevant ELISA values for the various peptides tested against sera from a population of healthy and infected subjects (see Example 2 starting at page 16 which states that 25 healthy persons and 30 people with culture proven allergic bronchopulmonary aspergillosis were tested). From this disclosure the skilled artisan learns what ELISA values are diagnostic in ascertaining whether or not a patient has aspergillosis. Clearly, any other peptide comprising SEQ ID NO: 1-6 that provides similar ELISA results would also be operable in the claimed invention.

The position of the Examiner is that the present specification does not enable one of skill in the art to determine, without undue experimentation, that a peptide larger than any one of SEQ ID NOS:1-6, is useful as a diagnostic tool for aspergillosis. That is, one of skill in the art cannot predict before running an experiment whether or not a protein comprising any one of SEQ ID NOS:1-6 will expose an epitope useful for that diagnosis.

It is Applicants' position that the Examiner is improperly relying upon a single *Wands* factor of predictability in the art, and has not fully considered the guidance in Applicants' present specification related to the presently claimed methods. ELISA is a well-known technique and the working Examples describe experiments for determining the usefulness of a short peptide of SEQ ID NO: 5, having seven amino acids, as a diagnostic reagent. Table 2 shows a range of ELISA values obtained from sera of infected patients and uninfected subjects using various peptides. Therefore, one skilled in the art would understand what constitutes a significant difference in ELISA values between infected patients and those not infected.

Further working examples provide similar information for peptides that append additional amino acids to each end of the short peptide of SEQ ID NO: 5. Therefore, the skilled artisan is shown how to determine if a polypeptide comprising a recited sequence is operable in the diagnostic method.

One skilled in the art would understand from the specification what experiments must be conducted and what results should be observed to determine if any particular peptide is operable in the invention. Furthermore, the state of the art, which encompasses typical ELISA assays, provides the knowledge of the details of how to conduct the required experiments. Finally, the sort of screening experiment described is expected to be conducted by the skilled artisan.

Therefore, such experimentation as may be necessary to perform the claimed invention throughout its scope is merely routine in nature and not considered as "undue".

Weighing the *Wands* Factors

Applicants respectfully submit that proper consideration of all of the *Wands* factors, and a proper weighing thereof, establishes enablement of the present invention as claimed. More specifically, considering all the features already cited (*i.e.*, quantitating an amount of peptide-IgG/IgE complexes), and in view of all information contained in the present specification (*i.e.*, teaching the appropriate starting material; the IgG and IgE levels in Table 2), working Examples (*i.e.*, Example 2 demonstrating peptides reacting with sera of aspergillosis patients), state of the art (*i.e.*, allergens and antigens of *Aspergillus fumigatus* have been identified by previous scientists), and the Rule 132 Declaration (previously submitted), one of skill in the art would know how to make and use the present invention without undue experimentation. Accordingly, Applicants respectfully submit that the claimed invention fully complies with the provisions of 35 U.S.C. § 112, first paragraph, and request that the Examiner to reconsider and to withdraw this rejection.

Conclusion

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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